(*1*) have been applied that derive from studies of atomic bomb survivors in Japan (*2–4*), acute postpartum mastitis patients treated with therapeutic X rays in New York (5, 6), and tuberculosis patients subjected to multiple fluoroscopes during air collapse therapy of the lung in Nova Scotia (7). None of these series, however, represents a population that has been exposed under conditions similar to those under which women undergoing periodic mammography, arc exposed, i.e., low-energy (25–50 kVp) and low-dose diagnostic X-ray examinations repeatedly performed over a number of years. The atomic bomb irradiation was a single whole-body exposure to high-energy $\gamma$ rays and neutrons. The mastitis patients were t rested for a breast disease by therapeutic X rays (175-270 kVp), and the radiation was delivered in one to several high-dose fractions over a period of about a week. The women with tuberculosis, on the other hand, received repeated low-energy (70–85 kVp) and relatively-low-dose fluoroscopic exposures to diagnostic X rays that continued for an average of 3–5 yr. The estimation of the radiation dose received by the Nova Scotia women was, however, so unreliable that the National Academy of Sciences chose the value of the postpartum mastitis study, six cases of breast cancer/106 woman-year-rad[5], as their best estimate of the absolute risk for radiation-induced breast cancer (*1*).

To augment existing data on risk estimates for the induction of breast cancer by ionizing radiation (*1–7*), a followup study was conducted of pulmonary tuberculosis patients in two Massachusetts hospitals who received repeated fluoroscopic examinations of the chest during air collapse treatments of the lung (pneumothorax and pneumoperitoneum) (8). To obtain information on the cumulative breast closes received by these patients, an extensive methodology, described in this report, was developed. These dose estimates were derived by abstracting information from medical records, interviewing physicians, contacting patients, measuring X-ray exposures from representative fluoroscopes, and applying an absorbed dose calculation scheme that employs a Monte Carlo radiation transport technique. Average absorbed breast doses were estimated for each patient fluoroscopically examined. On the basis of the observed frequency of breast cancers in the exposed population, estimates of breast cancer risk were made, and the resulting dose–response relationship was examined.

## SUBJECTS AND METHODS

### *Study Population*

Female patients who were discharged alive from two Massachusetts hospitals between 1930 and 1954 were studied (8). The numbers of pneumothorax or pneumoperitoneum treatments were determined from the hospital records, and 1047 women were designated as exposed individuals. The comparison group

[5] Absolute risk estimates as presented in the BEIR report (*1*) derive from the following calculations: $(O - E)/[(WY)(D)]$ where O = observed cases, $E$ = expected cases, $WY$ = woman-years at risk for breast cancer development., and $D$ = average breast dose in rad. The absolute excess risk estimate is specific for the years of followup included in the calculation. The postpartum mastitis estimate excludes the first 10 yr of followup, and is applicable for years 10 to 29 after initial exposure.

[redacted]

| | *Exposed group* | *Comparison group* |
|---|---|---|
| Number of women | 1047 | 717 |
| Fluoroscopy exams (av) | 102 | — |
| Years fluoroscoped (av) | 3.3 | — |
| Exams/year | 31 | — |
| Chest X rays (av) | 49 | 30 |
| X Rays/year as an: | | |
| In patient | 5.1 | 5.8 |
| Out patient | 2.1 | 1.8 |

consisted of 717 sanatorium patients who did not receive air collapse therapy and the associated repeated fluoroscope exposures.

For patients undergoing pneurnotherapy, air was injected into the pleural or peritoneal cavity in order to collapse the lung. For a period of several years, additional air was required every 1–3 weeks, and a fluoroscopic examination was conducted each time to determine the quantity of air needed to maintain the lung collapse. Table I shows the X-ray experience of the study

| | |
|---|---|
| Questionnaires sent to exposed subjects | 675 |
| Questionnaire responses | 543 |
| Questionnaire usable responses to position question | 341 (100%) |
| Omitted 96 | |
| Forgot 59 | |
| Not asked 47 (pilot questionnaire) | |
| Position when fluoroscopically examined | |
| Faced the M.D. | 213 (63%) |
| Faced X-ray tube | 56 (16%) |
| Varied | 72 (21%) |
| Rotated during fluoroscopy: 41 (12%) | |

TABLE III

Fluoroscopy Procedures as Determined by Physician Interview

| | |
|---|---|
| Number of physicians | 15 |
| Years as tuberculosis physician | |
| Average | 13 yr |
| Range | 2–25 yr |
| Patients given air without fluoroscopy | <1% |
| Patients fluoroscoped after refill | 1% |
| Patients fluoroscoped facing X-ray tube | 29% |
| Patients rotated during fluoroscopy | 20% |
| Fluoroscopy performed with shutters open | 69% |
| Opposite lung also scanned | 81% |
| Time for fluoroscopy examination | |
| Average | 15 sec |
| Range | 3–60 sec |

the patient questionnaire: 63% faced the physician during a fluoroscope, 16% faced the X-ray tube, and 21% had variable orientations (12% reported being rotated).

*Physician Interview*

To obtain detailed information on the actual conditions during the fluoroscopic examinations, 15 former tuberculosis physicians who had performed air collapse therapies and one former radiological technician were contacted. Tables III and IV present the results of these interviews. It was determined that (1) 29% of of the physicians fluoroscopically examined the patient with her chest (breasts) to the X-ray tube; (2) 69% conducted fluoroscopic examinations with the X-ray beam shutters wide open and 81% always scanned the opposite lung to determine whether the tuberculosis had spread; (3) the average time of a fluoroscopic examination was 15 sec (with responses ranging from 3 to 60 see); (4) 70 to 80

TABLE IV

X-Ray Field Conditions Selected to Be Consistent with Radiological Practice, 1930–1954

| *Projection* | *X-Ray field center* | | | *X-Ray field (width × height at image Receptor) (cm)* |
|---|---|---|---|---|
| | *Distance from phantom vertex (cm)* | *Distance from nearest anatonical landmark* | *Distance from phantom midline (cm)* | |
| Pneumothorax, shutters open | 42.4 | 7.6 cm above xiphoid process | 0 | 40.6 × 27.9 |
| Pneumothorax, shuttered beam | 42.4 | 7.6 cm above xiphoid process | 10 | 20.3 × 27.9 |
| Pneumoperitoneum | 52 | 2 cm below xiphoid process | 0 | 40.6 × 24.1 |
| Chest X ray | 42.4 | 7.6 cm above xiphoid process | 0 | 35.6 × 43.2 |

kVp and 5 mA were the usual 'machine parameters; and (5) 1 mm of aluminum filtration was added in 1948.

Information with regard to three different fluoroscopic field sizes was also obtained. In order to specify the X-ray fields on the phantom used in the absorbed dose calculations, the physicians were asked to sketch the body areas that would be included in the X-ray field during specific fluoroscopic examinations. The X-ray fields selected to be compatible with these sketches are summarized in Table IV.

*Fluoroscope Exposure Measurements*

Laboratory measurements were made on three representative fluoroscopy units: a Victor (G. E. ) Vertical Fluoroscope, Model B751 (1922), a Fisher Vertical Fluoroscope, Type X (1925), and a Picker Vertical Fluoroscope, Style T-10 (1935). One of the fluoroscopes had never been operated until a few years ago. Exposure rates at the fluoroscope panel and first half-value layers were determined for various peak kilovoltages and added aluminum filtrations. The experimental data are tabulated in Table V and presented in Fig. 1. The kilovoltages listed were measured using a sphere gap having 3.5-in. spheres, and the milliampere readings were checked for accuracy. Under similar operating conditions and at given kilovoltages and filtrations, all three systems provided essentially identical exposure rates.

From personal experience [E. D.T.), it is known that all fluoroscopes of this period used a 12- to 13-in. (30.5- to 33.0-cm) distance from the tube focal spot to the panel. Shorter distances could not be used since the high-voltage terminals were exposed and shorter distances would have led to arcing to the supporting structure. The 5-30 tube, later called the RB tube, was used in a lightproof lead glass shield. When the so-called autoprotective tube, the XP, became available, it was used because it provided better X-ray shielding. A mounted cone was provided that placed the focal spot at the same distance from the panel as was the case with the RB tube.

The RB tube, when operated on self-rectified equipment, could be operated continuously at 85 kVp and 5 mA for 6 min in any 36-rein interval. Operation at lower kilovoltages would permit slightly longer operating times; however, long exposures were impossible as they would permanently damage the fluoroscope tube.

Table V and Fig. 1 can be used to determine patient exposure if operating conditions are known. For example, if a fluoroscope were operated with no added filtration at 75 kVp and 5 mA for an average exposure time of 15 see, the patient entrance skin exposure measured free-in-air would be (10.2 R/mA-min) (5 mA) (0.25 rein) = 12.75 R.

A fluoroscope used to monitor the lung collapse of the Massachusetts women in this study was also located in a private physician's office. Exposure rates determined for various machine settings were within 6% agreement with the controlled fluoroscopic measurements made in the laboratory.

The exposure measurements were summarized into average conditions for each of two time periods to be consistent with fluoroscopic practice before and after

TABLE V

Exposure Rate at Panel, First HVL, and Kilovolt Peaks for Selected Autotransformer Settings and Added Aluminum Filtration[a]

| *Autotransformer setting* | *kVp* | *Added filter (mm Al)* | *First HVL (mm Al)* | *Exposure rate* | |
|---|---|---|---|---|---|
| | | | | *R/min* | *R/mA-min* |
| 4 | 58 | 0 | 0.7 | 30.2 | 6.05 |
| | | 0.5 | 1.05 | 18.2 | 3.65 |
| | | 1.0 | 1.3 | 12.7 | 2.55 |
| | | 2.0 | 1.65 | 7.5 | 1.5 |
| | | 3.0 | 2.0 | 4.8 | 0.96 |
| 8 | 63 | 0 | 0.75 | 36.2 | 7.2 |
| | | 0.5 | 1.15 | 22.2 | 4.45 |
| | | 1.0 | 1.4 | 15.7 | 3.1 |
| | | 2.0 | 1.75 | 9.6 | 1.9 |
| | | 3.0 | 2.15 | 6.6 | 1.3 |
| 12 | 68 | 0 | 0.8 | 42.0 | 8.4 |
| | | 0.5 | 1.15 | 26.7 | 5.35 |
| | | 1.0 | 1.5 | 18.9 | 3.8 |
| | | 2.0 | 1.8 | 11.7 | 2.35 |
| | | 3.0 | 2.35 | 8.1 | 1.6 |
| 18 | 75 | 0 | 0.9 | 51.2 | 10.2 |
| | | 0.5 | 1.25 | 32.9 | 6.6 |
| | | 1.0 | 1.55 | 24.1 | 4.8 |
| | | 2.0 | 2.0 | 15.8 | 3.15 |
| | | [illegible] | [illegible] | [illegible] | [illegible] |
| | | 1.0 | 1.7 | 31.6 | 6.3 |
| | | 2.0 | 2.2 | 21.1 | 4.2 |
| | | 3.0 | 2.75 | 15.2 | 3.05 |

[a] General Electric Vertical Fluoroscope 5 mA, (8 × 10)-in. field at panel.

1948 (Table VI). The exposure rate at the panel for all patients fluoroscopically examined before 194S was assigned the value of 51.2 R/rein for an unfiltered X-ray beam. A panel exposure rate of 24.1 R/rein was assigned for a l-mm added aluminum-filtered beam for all patients receiving fluoroscopes during and after 1948.

### *Absorbed Dose in the Breast*

Estimates of absorbed dose in the breast were derived from a Monte Carlo radiation transport technique, a method that simulates and records the energy deposition of X-ray photons as they undergo physical interactions in an anthropomorphic phantom (9). When the technique is applied to simulate the

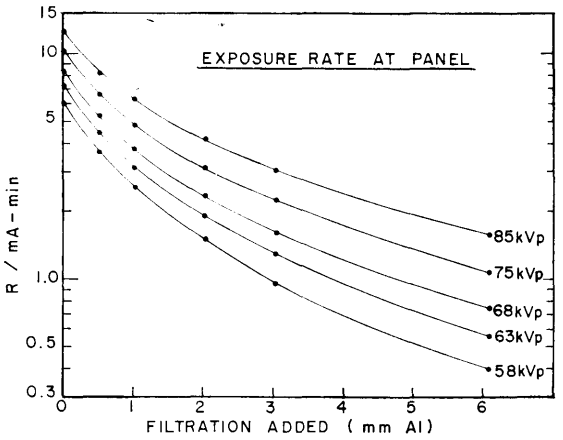


FIG. 1. Exposure rate (R/mA-min) at fluoroscope panel for various kilovoltage and filtration conditions.

interaction of diagnostic X rays in human tissue, the physical processes treated are the photoelectric effect and Compton scattering. The initial energies of the X-ray photons used during air collapse fluoroscopes were less than 100 keV.

The anthropomorphic phantom represents a reference human and is heterogeneous. It consists of skeletal, lung, and tissue regions with corresponding compositions and densities. The important human organs are mathematically formulated within the phantom and are the interaction sites of interest. Energy depositions are accumulated at these sites. The average absorbed dose in the organ of interest is obtained directly by dividing the accumulated energy by the mass of the organ.

For the present study, the phantom was modified to include the female breasts as described below. X-ray spectral distributions representing the beam qualities of interest were also employed as well as exposure geometries used during the fluoroscope examinations. The details of the Monte Carlo technique and the phantom, as applied generally with diagnostic X-ray photon energies, have been previously described (9).

Two categories of patient breast size were modeled in the anthropomorphic phantom, an adolescent and an adult. The shape of the breast was simulated by

TABLE VI

Fluoroscopy Conditions Selected to Be Consistent with Pneumotherapy Practices

| | |
|---|---|
| Beam quality | 75 kVp |
| X-Ray tube current | 5 mA |
| Tube-to-panel distance | 33 cm |
| Exposure rate at panel | |
| Before 1948, unfiltered beam | |
| (HVL = 0.9 mm Al) | 51.2 R/min |
| After 1948, 1 mm aluminum added filtration | |
| (HVL = 1.55 mm Al) | 24.1 R/min |

one-half an ellipsoid of revolution attached to the chest wall of the existing phantom with the following dimensions: adolescent breast, 3-cm distance from chest wall to nipple and 3.75-cm diameter at the chest wall, 22.3 g each; adult breast, 6-cm distance from chest wall to nipple and 7.5-cm diameter at the chest wall, 179 g each. The remainder of the phantom serves as a backscattering medium in the AP orientation and as a shielding medium (20 cm thick) in the PA orientation. The composition of all breasts was that of average glandular tissue: 10.5% hydrogen, 23.0% carbon, 2.3% nitrogen, 63.2% oxygen, and various smaller percentages of other trace elements (9). As a result of physician interviews and the relatively young age of most patients, it was decided that these assumptions were consistent with the observation that patients with sufficiently serious tuberculosis to require pneumothorax therapy were generally thin and deficient in both subcutaneous and mammary fat. If the composition of breast were assumed to include a proportion of mammary fat (e. g., 50% adipose and 50% glandular), the resulting decrease in absorbed dose would be less than 15% for all conditions.

To simulate the beam qualities selected as representative of patient treatment (Table VI), X-ray spectra were measured on laboratory X-ray sources using germanium detectors (10). The kilovolt peak and HVL values were matched with those in Table VI, resulting in the X-ray spectra tabulated in Table VII.

The absorbed dose (rad) in the breast per 1 R of entrance skin exposure (free-in-air) was calculated for each breast for 16 selected exposure situations (Table VIII).[6] The absorbed dose in the breast is defined as the total energy deposited in the breast volume divided by the total breast mass.

These 16 selected exposure situations (Table VIII) take into account the following factors: (1) 2 beam qualities (Table VI); (2) 2 patient orientations (AP, radiation incident on the anterior skin surface, or PA, radiation incident on the posterior skin surface); (3) 2 breast sizes (adult or adolescent), and (4) 4 X-ray field sizes and locations (Table IV).

For example, an adult woman facing the X-ray tube (AP) before 1948 (unfiltered, 0.9 mm Al HVL beam) would receive a right-breast dose of 0.412 rad and a left-breast dose of 0.005 rad for each 1 R of entrance skin exposure if the physician shuttered the X-ray beam during a right-lung pneumothorax fluoroscope.

[6] Recent experimental measurements (*13*) of absorbed dose in the breast utilizing an Alderson–Rando phantom, Mix-D breast simulations (as described above) and multiple locations of lithium fluoride dosimeters (TLD-100) are in good agreement with the Monte Carlo computed breast dose values. The X-ray beam qualities, geometries, and exposure conditions were maintained constant for both the experiment and computations. For the AP view, in which the breast is directly exposed, the absorbed dose is about 0.5 rad/R and agreement was within 2%. As the AP view is the overwhelming cent ributor of breast dose, this comparison is the most meaningful. For the PA view, in which the X rays are attenuated by 20 cm of intervening inhomogeneous tissues, the absorbed dose is about 0.02 rad/R and agreement was poorer (20 to 50%). In the light of experimental and computational uncertainties involved with the reduced dose from a PA view and also the differences in the composition of the experimental and mathematical phantoms, the discrepancy is not surprising. Regardless, the PA view contributes only a small fraction of the total breast dose among those patients

TABLE VII

X-Ray Spectra Used in Absorbed Dose Calculation

| *Photon energy (keV)* | *Relative number of photons*[a] | |
|---|---|---|
| | *75 kVp, 0.9 mm Al HVL* | *75 kVp, 1.55 mm Al HVL* |
| 8 | 0.0002 | 0.0026 |
| 10 | 0.0650 | 0.0099 |
| 12 | 0.1498 | 0.0294 |
| 14 | 0.3093 | 0.0812 |
| 16 | 0.5647 | 0.2053 |
| 18 | 0.7705 | 0.3949 |
| 20 | 0.8989 | 0.5788 |
| 22 | 0.9810 | 0.7509 |
| 24 | 1.0000 | 0.8750 |
| 26 | 0.9907 | 0.9558 |
| 28 | 0.9492 | 1.0000 |
| 30 | 0.8986 | 0.9989 |
| 32 | 0.8435 | 0.9896 |
| 34 | 0.7893 | 0.9599 |
| 36 | 0.7292 | 0.9227 |
| 38 | 0.6704 | 0 8701 |
| 40 | 0.6226 | 0.8163 |
| 42 | 0.5704 | 0.7641 |
| 44 | 0.5165 | 0.7038 |
| 46 | 0.4707 | 0.6441 |
| 48 | 0.4303 | 0.5919 |
| 50 | 0.3922 | 0.5396 |
| 52 | 0.3512 | 0.4897 |
| 54 | 0.3169 | 0.4439 |
| 56 | 0.2822 | 0.3959 |
| 58 | 0.2741 | 0.3581 |
| 60 | 0.2423 | 0.3199 |
| 62 | 0.1891 | 0.2557 |
| 64 | 0.1610 | 0.2065 |
| 66 | 0.1351 | 0.1702 |
| 68 | 0.1144 | 0.1250 |
| 70 | 0.0764 | 0.0701 |
| 72 | 0.0468 | 0.0274 |
| 74 | 0.0100 | 0.0075 |

[a] Normalized to 1 photon at peak energy.

*Fluoroscope Doses*

To determine cumulative patient breast doses from fluoroscopic examinations,

TABLE VIII

Breast Dose (Expressed as rad per 1 R of Entrance Skin Exposure Free-in-Air) for 16 Selected Radiologic Conditions

| *Breast size* | *Beam quality (Table VI) (mm Al HVL)* | *Field size* | *Patient orientation with respect to X-ray tube* | *Average breast dose (rad/R)* | |
|---|---|---|---|---|---|
| | | | | *Right breast* | *Left breast* |
| Adult | 0.9 | Shuttered pneumothorax | AP[a] | 0.412[b,c] | 0.005 |
| Adult | 1.55 | Shuttered pneumothorax | AP | 0.456[b] | 0.007 |
| Adult | 0.9 | Unshuttered pneumothorax | AP | 0.482 | 0.482 |
| Adult | 1.55 | Unshuttered pneumothorax | AP | 0.559 | 0.559 |
| Adult | 1.55 | Pneumoperitoneum | AP | 0.012 | 0.012 |
| Adolescent | 0.9 | Shuttered pneumothorax | AP | 0.698[b] | 0.004 |
| Adolescent | 1.55 | Shuttered pneumothorax | AP | 0.794[b] | 0.005 |
| Adolescent | 0.9 | Unshuttered pneumothorax | AP | 0.769 | 0.769 |
| Adolescent | 1.55 | Unshuttered pneumothorax | AP | 0.810 | 0.810 |
| Adult | 0.9 | Shuttered pneumothorax | PA | 0.015[b] | 0.002 |
| Adult | 1.55 | Shuttered pneumothorax | PA | 0.022[b] | 0.002 |
| Adult | 0.9 | Unshuttered pneumothorax | PA | 0.017 | 0.017 |
| Adult | 1.55 | Unshuttered pneumothorax | PA | 0.022 | 0.022 |
| Adult | 0.9 | Chest X-ray | PA | 0.043 | 0.043 |
| Adult | 1.55 | Chest X-ray | PA | 0.048[d] | 0.048 |
| Adult | 1.55 | Pneumoperitoneum | PA | 0.005 | 0.005 |

[a] Patient faces X-ray tube during AP orientation.
[b] In presence of right lung pneumothorax.
[c] The coefficients of variation for calculated rad/R values of 0.412 or greater are 1.5 to 4.0%.
[d] The coefficients of variation for calculated rad/R values of 0.048 or less are 9.0 to 30.0%.

consistent with the adult breast size. Examinations before 1948 were assigned exposure rates and absorbed doses for an unfiltered beam; fluoroscopes during and after 1948 were assigned corresponding values for a filtered beam (Table VI). The field size was determined by the type of examination (Table IV).

Except for the few questionnaire respondents who recalled their orientation with respect to the fluoroscope X-ray source, individual orientations could not be determined. Considering the physician and patient questionnaire responses (Tables II, III) it was decided to assume that 25% of all examinations were

performed in the AP position (with the patient facing the X-ray tube) and 75% in the PA position. During a unilateral lung collapse, both breasts were assumed to be in the X-ray beam 81% of the time (unshuttered) (Table 111), whereas 19% of the time only one breast was assumed exposed (shuttered). In the latter case, average breast doses were computed by adding the dose received by the exposed breast and the scatter dose received by the opposite breast and dividing by 2. For the few cases in which both lungs were collapsed (bilateral), both breasts were exposed 100% of the time during fluoroscope. The average time for a fluoroscope examination was assumed to be 15 sec.

If an adult woman had received 10 pneumothorax examinations before 1948, her estimated cumulative breast dose would be computed as: [(10 exams) (51.2 R/rein) (0.25 rein/exam)] {0.81 [0.25(0.482 rad/R) + 0.75(0.017 rad/R)] + 0.19[0.25(0.412 + 0.005 rad/R)/2 + 0.75(0.015 + 0.002 rad/R)/2]} = 15.2 rad.

It should be noted that "average" breast doses were computed for each individual on the basis of the best estimates of average orientation and average fluoroscopy practices obtained through patient and physician enquiry. As individual breast doses could be estimated for only a small number of patients, it was decided to compute average doses for all individuals. Initially an attempt was made to utilize individually identifiable information but it was unsuccessful. Many of the 269 patients with presumed known orientation were treated by physicians who had died, and therefore fluoroscope information was unattainable. It was also common for patients institutionalized for many years to have been treated by several physicians, not all of whom were interviewed. Coupled with the obvious difficulty in relying on individual patient and physician memories of 20 to 45 yr ago, it seemed prudent to use the "averuge" values of all patient and physician responses for estimating breast doses for all patients.

## RESULTS

### *Breast Cancer and Number of Fluoroscopic Examinations*

Fifty-six histologically confirmed breast cancer cases among all study subjects were ascertained. Figure 2 shows the standardized incidence rates of breast cancer, adjusted for age at exposure and duration of followup, as a function of

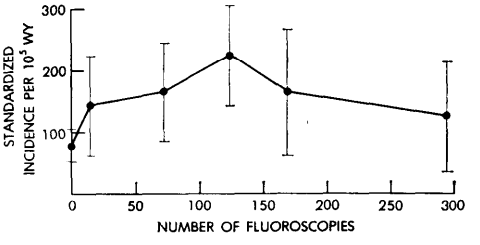


FIG. 2. Standardized incidence of breast cancer per 100,000 woman-years (WY) at risk adjusting for age at exposure and duration of followup, by number of fluoroscopic examination; 80% confidence limits presented.

TABLE IX

Observed and Expected Breast Cancer Cases and Women-Years at Risk by Average Breast Dose

| | *Average breast dose (rad)* | | | | | | *Total*[a] |
|---|---|---|---|---|---|---|---|
| | *0* | *1–99* | *100–199* | *200–299* | *300–399* | *400+* | |
| *Mean dose (rad)* | *0* | *32* | *151* | *242* | *344* | *574* | |
| Number of women | 717 | 469 | 251 | 177 | 65 | 62 | 1047 |
| Breast cancer cases | | | | | | | |
| Observed | 15 | 10 | 12 | 12 | 3 | 4 | 41 |
| Expected[b] | 14.1 | 9.6 | 5.7 | 4.8 | 1.5 | 1.1 | 23.3 |
| Woman-years at risk (WY) | 19,025 | 10,990 | 7097 | 5584 | 2020 | 1735 | 28,011 |
| Standardized incidence per $10^5$ WY[c] | 79 | 109 | 165 | 225 | 144 | 354 | 159 |

[a] Includes unknown dose category, and excludes 0-rad comparison patients.

[b] Expected values computed using Connecticut age–calendar year specific breast cancer incidence rates.

[c] Comparing the exposed patients with the 0-rad comparison patients, adjusting for age at exposure and duration of followup.

number of fluoroscopic examinations (8). The comparison patients were used as the standard. An increased risk is suggested for those receiving less than 50 fluoroscopes, but the increase is not statistically significant ($P$ = 0.5, 1 tail). A decrease in risk among those receiving 150 or more fluoroscopes is also suggested. Distribution of risk by number of fluoroscopes, however, fails to take into account the previously mentioned factors that contribute to the magnitude of absorbed dose in the breast.

### *Breast Cancer and Cumulative Absorbed Dose*

Observed and expected breast cancer cases and woman-years at risk as a function of cumu ative breast dose (rad) are presented in Table IX, and standard-

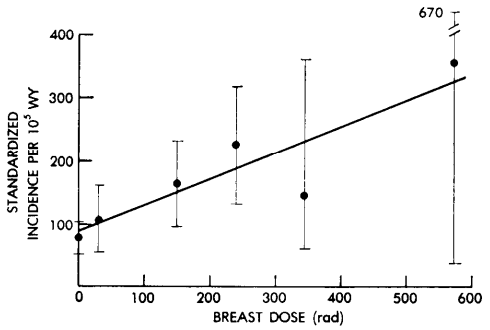


FIG. 3. Standardized incidence of breast cancer per 100,000 woman-years (WY) at risk adjusting for age at exposure and duration of followup, by estimated cumulative breast dose. Best-fitting least-squares line and 80% confidence limits presented.

ized breast cancer incidence rates in Fig. 3. No decrease in risk at high doses (574 rad) is apparent, and a dose-response relationship that increases linearly or otherwise continuously with increasing dose is not inconsistent with the data [$X_1^2$ (trend) = 7.6, $P$ = 0.003]. The confidence limits are wide, however, and other patterns are possible. (Figure 3 differs somewhat from a previously published dose-response curve (8) in that incidence rates of the "nonexposed" tuberculosis patients are used as the standard instead of Connecticut Tumor Registry rates.)

*Risk Estimate*

A single fluoroscopic examination was estimated to result in an average absorbed dose to the breast of 1.5 rad, and each individual received an estimated cumulative breast dose of approximately 150 rad on the average. The Massachusetts women in this study, living 10 yr or more since first fluoroscopic exposure, are estimated to have a breast cancer risk of 6.2 radiation-induced breast cancer cases per million woman-year-rad, with 90% Poisson confidence limits of 2.8 and 10.7 cancers/$10^6$ WY-rad (Table X).

It is important to examine each assumption made in deriving the above risk

TABLE X

Average Breast Doses and Resulting Risk Estimates as a Function of the Assumptions Regarding Fluoroscopic Practice

| *Assumption* | *Estimated average breast dose per subject (rad)* | *Risk estimate*[b] *CA/106 WY-rad* |
|---|---|---|
| Best estimate[a] | 149 | 6.2 |
| Breast size | | |
| Adolescent (3 cm) | 208 | 4.5 |
| Adult (6 cm) | 136 | 6.8 |
| Aluminum beam filtration | | |
| Inherent, only | 166 | 5.6 |
| 1 mm added | 90 | 10.3 |
| X-Ray field size | | |
| Unshuttered | 167 | 5.5 |
| Shuttered | 75 | 12.4 |
| Time for exam (see) | | |
| 20 | 199 | 4.7 |
| 10 | 100 | 9.3 |
| 5 | 50 | 18.5 |
| Patient orientation (% facing X-ray tube) | | |
| 100 | 543 | 1.7 |
| 30 | 175 | 5.3 |
| 20 | 123 | 7.5 |
| 0 | 18 | 51.5 |

[a] Assumption: Adolescent breast size for those under 17 yr of age at first exposure; 1 mm Al added in 1948; 81 % of the exams performed unshuttered; 15-sec exam time; 2570 of the exams performed with patients facing the X-ray tube.

[b] Computed as (O - $E$)/{(WY) (dose)), i.e., (38 - 20.85)/{ (18, 511) (estimated dose). } (The first 10 yr of observation have been excluded.)

estimate in order to determine-the range of possible risk estimates that could result if different fluoroscope conditions were assumed. Table X lists the average breast doses and resulting risk estimates as

Similarly, the estimated average breast dose per fluoroscopic examination was calculated by adding the doses received by both breasts and dividing by 2. This concept of average dose to the total organ system has been used in two previous human studies (*5,11*). Nevertheless, the concept may be questioned, particularly when the breasts are unevenly or partially irradiated. In addition, if the distribution of radiosensitive tissue in the breast is not uniform, computing the radiation dose using total breast volume may not be the most appropriate approach. No other method of estimating breast dose, however, was deemed practical.

Table XI compares the findings of the current Massachusetts fluoroscope study with the three previously mentioned studies. The risk estimate for the Massachusetts tuberculosis patients is comparable with the two studies of Western women but about three times larger than the estimate from the Japanese population exposed to atomic radiation. One explanation is a variation in genetic susceptibility. Alternative explanations for this difference might be that the Japanese risk estimate is diluted because of the inclusion of the low-risk post-exposure years 5 to 9 in the risk computation. Because the Japanese study has a maximum period of observation of 25 yr, it is also possible that the risk estimate will increase with the passage of time, as suggested in the current study (8). These two factors alone could possibly explain the difference in risk estimates. If the risk estimate for the Massachusetts women in our study were calculated considering only years 5 to 24 of followup, the absolute risk estimate would have been 3.1 cases/$10^6$ WY-rad, in close agreement with the Japanese estimate of 2.5 cases/$10^6$ WY-rad.

The Western studies also involved populations of women whose mean ages at first exposure were 7–9 yr younger than the Japanese women. If age at exposure is inversely related to breast cancer risk (8), the older atomic bomb victims may in fact be at lower risk. The Japanese women also received "whole-body" radiation exposure, and if the resulting ovarian irradiation had a protective effect on breast cancer development, the risk estimate obtained would be lower than the estimate from those studies involving partial-body irradiation. In studies of women undergoing radiation cast ration (12), significant decreases in death due to breast cancer have been observed that could be attributable to ovarian irradiation.[8]

Although the absolute risk estimate derived from our study of Massachusetts fluoroscope patients can be supported with some confidence, a number of dose–response relationships could be consistent with the data. The variation of breast cancer incidence rate by the number of fluoroscopic examinations suggests a falloff of risk at the higher cumulative doses. In the Nova Scotia fluoroscope study, no falloff was seen and breast cancer incidence increased with increasing numbers of fluoroscopic examinations up through the maximum average number of 450 (*1*). No falloff was observed in the present study either, when the breast cancer incidence rate was expressed as a function of cumulative patient breast dose (rad) rather than the number of fluoroscopic examinations. Conversion to cumulative breast dose included the effect of important variables such as orienta-

[8] In animal studies, however, mammary neoplasia can be increased when only the ovaries of mice are irradiated (16); whereas, no effect on mammary neoplastic development attributable to ovarian irradiation is apparent following "whole-body" radiation exposure of rats (*16*).

TABLE XI

Risk Estimates for Breast Cancer Induction by Radiation and Comparisons with Other Studies

| | *Number irradiated* | *Woman-years used for risk calculation* | *Type of radiation* | *Duration of exposure* | *Age at exposure range (mean)* | *Breast dose in rad range (mean)* | *Time after irrad. on which risk estimates are based (years)* | *Relative risk (O/E)* | *Cancers induced per $10^6$ WY-rad (90% CL)* |
|---|---|---|---|---|---|---|---|---|---|
| Atomic bomb survivors[a] (*1, 3, 4*) | 11,968 | 235,345 | Gamma ray and neutron | Less than 10 sec | 10+ (34) | 10–450 (61) | 5–24 | 82/48.5 =1.7 | 2.5 (1.3, 3.6) |
| Nova Scotia fluoroscopy series (*1, 6*) | 243 | 3,708 | Diagnostic X ray, 70–85 kVp | Weeks to years | 0–60+ (26) | 50–7,000 (1215) | 10–30 | 10.5 | 8.4[b] |
| Mastitis patients (*1, 5, 12*) | 606 | 9,301 | Therapeutic X ray, 175–250 kVp | Minutes to weeks | 15–44 (27) | 40–1,200 (247) | 10–34 | 36/16.2 =2.2 | 8.3 (3.1, 16.0) |
| Current Massachusetts fluoroscopy study | 1,047 | 18,511 | Diagnostic X ray, 70–85 kVp | Days to years | 5–55 (25) | 1–1,027 (150) | 10–44 | 38/20.9 =1.8 | 6.2 (2.8, 10.7) |

[a] Women over 10 yr of age at irradiation who received greater than 9 rad of breast kerma dose.
[b] Confidence limits (CL) cannot be calculated.

tion, beam filtration, and type of examination. The sample size and the associated confidence limits on the breast cancer incidence rates are such that dose-response functions other than linear could be compatible with the data. Although no clear-cut dose–response function is evident, the data are consistent with linearity and it appears prudent to assume a linear relationship for the purpose of radiation protection and public health considerations (*1*).

When comparing the exposed patients with the comparison patients and adjusting for age at exposure and duration of followup (Table IX), it is interesting that a risk associated with breast doses under 100 rad is suggested: The standardized incidence rate of breast cancer among those receiving an average of 32 rad is $109/10^5$ versus $79/10^5$ WY for the comparison patients. This increase, however, is not statistically significant ($P$ = 0.47, 1 tail). When Connecticut incidence rates are used to compute expected breast cancer cases (Table IX), no excess breast cancer is apparent among those receiving less than 100 rad (10 cancers observed and 9.6 expected). These data, however, should not be interpreted to mean that there is *no* risk for breast cancer induction at these dose levels. The sample size of 469 women and the average breast dose of 32 rad may have been too small to detect a statistically significant increased risk. On the basis of a risk estimate of 6.2 cancers/$10^6$ WY-rad, an excess of 1.4 radiogenic breast cancers would have been expected for these 469 women. There is no statistically significant difference between the observed 10 cases and the predicted (9.6 + 1.4) = 11 cancers based on the radiation risk estimate.

Data from the previous fluoroscope study of Nova Scotia tuberculosis patients were consistent with a linear dose–response relationship between breast cancer incidence and high total breast doses attained from many individual low-dose fractions (*1*). Because all the Nova Scotia women faced the X-ray tube during fluoroscope examination, the cumulative breast doses were great, averaging 1215 rad. The range of cumulative breast doses for the Massachusetts patients in our study (150-rad average), however, is approximately one magnitude lower than that for the Nova Scotia series. The results of the two studies, with regard to the shape of the dose-response curve and the computed breast cancer risk estimates, are compatible. This suggests that for low-dose fractionated exposures, the breast cancer risk per rad is similar over a wide range of total cumulative doses.

The fluoroscope studies also present overall radiation risk estimates that are similar to those derived from studies involving single or few radiation exposures (2-5). The repeated fluoroscopic exposures, however, were delivered over a period of years, allowing cellular repair and repopulation to occur. Since these multiple low-dose exposures might be expected to produce fewer deleterious effects than a single exposure of the same total dose (*1*), the fact that they do not suggests that the radiation damage is cumulative. When assessing the possible radiation risk associated with repeated low-dose mammography exposures, it appears prudent to assume that the risk is present at the low dose levels involved and that the total risk will be proportional to the total radiation dose received during the lifetimes of the women exposed,

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